MH28 21

THE OHIO STATE UNIVERSITY
COLUMBUS

DEPARTMENT OF MEDICINE
OFFICE AND RESEARCH LABORATORIES
KINSMAN HALL

January 22, 1940

Dear Dr. Heidelberger:

At luncheon in New York at the meeting of the Research Committee of the National Tuberculosis Association, Dr. Sabin told me that she had discussed with you some of the things which we would like to do in carrying further her observations on the relationship of phagocytosis of your synthetic azo dye antigen to anti-body formation. I had hesitated to say anything to you about it because I know how many uses you have for the products of your chemical synthesis and doubtless many demands for material, just as does Anderson and other biochemists. Dr. Sabin told me, however, that you were interested sufficiently so that I might feel free to place the matter quite frankly before you for your consideration. I regret that I did not have the opportunity, after this conversation with her, to talk with you directly, which is what I had hoped might be possible during the trip to New York.

During this current year we have been interested particularly in attempting to secure further information relative to the separate or mutual identity of so-called clasmatocytes and monocytes. It has always seemed to me that various pathologic reactions tend to accentuate the differences in reaction as exemplified by the two morphologic states which formed the original basis for the separation of these cell types. We have therefore set up a microcinematographic outfit, after having studied for several years the invitro cultures of these cells from both animal and human sources, and are attempting to accumulate evidence from a functional and cell motility standpoint, which may throw further light on the subject.

When Dr. Sabin told me of her work with the dye antigen from your laboratory, it seemed to me that there were new possibilities associated with color microphotography for the accumulation of further proof of her intriguing hypothesis.

She tells me that now you have not only the egg albumin-dye molecules, but also have been able to "mark" a specific antigen of the stretococcus. Would you think that by comparing and contrasting the degree and specificity of phagocytosis and the period of time necessary for the breakdown of the synthetic molecule and the appearance of anti-bodies, we might demonstrate that the monocyte or the clasmatocyte respectively might show a greater efficiency in the handling of one as contrasted with the other?

Dr. Houghton, who has been doing our tissue culture and organ culture work for several years, had his basic training with Dr. Carrell, and he has been successful for example, in culturing in vitro a human parathyroid gland removed at operation, and after cultivating it in the gradually increasing concentrations of the recipient patient's serum with hypoparathyroid tetany, has returned it to the surgeon for successful re-implantation with complete functional results, a la Harvey Stone. In his in vitro cultivations of thyroid tissue, he has been able to demonstrate the elaboration of thyroxin according to Carrell's technic.

Could we not hope to take explants of either spleen or omental milk spots 24 to 72 hours after in vivo inoculation with your antigen, and determine any specific anti-body formation which might occur thereafter in vitro? Would it not be possible, also, to introduce the antigen directly into cultures of cells, observe phagocytosis, if and when it occurs, and follow the anti-body content of the nutrient medium which would be removed from the cultures from time to time? May the material be prepared sterilely?

There are a number of technical angles to the problem, both from your side and from ours, which it might be desirable to consider more fully in a personal conference, if you would feel it advisable. I should appreciate your frank reaction to this whole matter, and I assure you that both Dr. Houghton and myself are quite anxious for your constructive criticism of the general idea.

If the conception does not seem too entirely without sufficient basis for further exploration, and if the work could be facilitated by our coming and discussing the matter in detail with you before it is carried into actual experimental action, we would try and arrange to meet your convenience. The utmost conservation of materials would be one of the main considerations.

Anticipating hearing from you, and with best personal regards,

Very cordially,

Charles A. Doan, M. D.
Professor of Medicine

D-H

Dr. Michael Heidelberger,
Columbia University Medical Center,
New York City